

### **REMARKS**

Claims 88, 93-99, 102-110, 128, 134, and 138 were pending in the application; Claims 93-95 and 97 being cancelled and new Claims 154-156 being added with this amendment, Claims 88, 96, 98, 99, 102-110, 128, 134, 138 and 154-156 are pending in the application.

The amendments to Claims 88, 96, 103 and 109 incorporate elements of other claims into the amended claims, and find support in the specification at, for example, paragraph 12 on page 4, paragraph 27 on page 9, paragraph 41 on page 15; paragraph 93 on pages 38-39; paragraph 98 on page 40; in Claims 9-11 as originally filed; and elsewhere in the specification.

New Claims 154-156 recite a vector, a host cell comprising a vector, and a kit, all of which comprise a novel, useful isolated polynucleotide as recited in amended Claim 96. Support for such vectors, host cells, and kits may be found in the specification, for example, a page 10, paragraphs 28 and 29; pages 41 – 42; paragraphs 100-102; page 44, paragraphs 106-107; and elsewhere in the specification.

No new matter is added by way of the amendments and new claims.

Claims 88, 93-99, 102-110, 128, 134 and 138 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabling a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Claims 88, 93, 99 and 102-110 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Prasher et al., (Gene 111, 229-233 (1992), hereafter "Prasher"). Claims 88, 93, 99, 102-110, 128 and 134 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Heim et al. (PNAS 91, 12501-12504 (1994), hereafter "Heim"). Claims 88, 93-95, 99, 102-110, 128 and 134 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by Tsien et al. (U.S. Patent No. 6,140,132, hereafter "Tsien"). Applicants respectfully traverse the rejections to the claims.

### **The rejections under 35 U.S.C. §112, First Paragraph**

Claims 88, 93-99, 102-110, 128, 134 and 138 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabling a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Applicants gratefully acknowledge the Examiner's statement (page 3, paragraph 5, lines 2-13 of the paragraph) that the specification is "enabling for a polynucleotide encoding at least one monomer of a non-oligomerizing tandem fluorescent protein, wherein the fluorescent protein comprises a first monomer of a green fluorescent protein (GFP) or a fluorescent protein related to GFP operatively linked to at least a second monomer of a GFP or a fluorescent protein related to GFP, wherein the amino acid sequence of the monomer is defined (e.g., the A206K, L221K or F223R mutant of SEQ ID NO:6 or 10), and wherein the propensity of the tandem fluorescent protein to form intermolecular oligomer[s] is reduced or inhibited; a vector or host cell comprising the polynucleotide; a kit comprising the nucleotide; or, a polynucleotide encoding at least a monomer of a fusion protein, wherein the fusion protein comprises the non-oligomerizing tandem fluorescent protein operatively linked to at least one polypeptide of interest, wherein the monomer and the polypeptide of interest (e.g., polyHis tag) are defined; and the polynucleotide encoding the GFP from *Aequorea Victoria* as shown in the prior art."

As amended, Claim 88 is directed to a polynucleotide encoding at least a first monomer of a non-oligomerizing tandem fluorescent protein, the first monomer comprising a mutation of an amino acid residue corresponding to A206K, L221K, F223R, or a combination thereof of SEQ ID NO: 6 or SEQ ID NO:10, as described by the Examiner as being enabled as discussed in the present Office Action. Similarly, each of the claims dependent on Claim 88 (e.g., Claims 99, 102-110, 128, 134, and 138) also recite subject matter enabled in the specification by the disclosure at, for example, page 51, paragraph 122; pages 39-43, paragraphs 95-105; the Examples; and elsewhere in the specification.

Applicants also gratefully acknowledge the Examiner's statement (page 5, paragraph 2, lines 2-5 of the paragraph) that the specification "has shown the A206K, L221K and F223R mutants of SEQ ID NOs:6 and 10 are non-oligomerizing fluorescent protein (Example 1), where the replacement of the hydrophobic residues A206, L221 and F223 with residues containing positively charged side chains eliminates dimerization."

As amended, Claim 96 is directed to a polynucleotide encoding at least a first monomer of a non-oligomerizing tandem fluorescent protein, the first monomer comprising a mutation substituting an amino acid having a positively charged side-chain for an amino acid corresponding to A206, L221, F223 or a combination thereof of SEQ ID NO:2, as described by the Examiner as being enabled as discussed in the present Office Action. Similarly, each of the claims dependent on Claim 96 (e.g., Claims 98, and 154-156) are enabled in the specification by the disclosure at, for example, page 51, paragraph 122; pages 39-43, paragraphs 95-105; the Examples; and elsewhere in the specification.

Thus, Claims 88, 99, 102-110, 128, 134, and 138 are believed to be enabled, reciting at least a first monomer comprising a defined mutation corresponding to A206K, L221K, F223R, or a combination thereof of SEQ ID NO: 6 or SEQ ID NO:10. Claims 96, 98 and 154-156 are also believed to be enabled, reciting at least a first monomer comprising a defined mutation substituting an amino acid with a positively charged side-chain for an amino acid corresponding to A206, L221, F223 or a combination thereof of SEQ ID NO:2. Accordingly, Applicants believe the rejections of Claims 88, 93-99, 102-110, 128, 134, and 138 under 35 U.S.C. §112, first paragraph, to be overcome.

#### **The Rejections under 35 U.S.C. § 102**

Claims 88, 93, 99 and 102-110 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Prasher. Claim 93 stands canceled in the present amendment, so that its rejection is moot. Anticipation under 35 U.S.C. §102 requires that "every element of the claimed invention be identically shown in a single reference." (*In*

*re Bond*, 910 F.2d 831,832 (Fed. Cir. 1990)). However, Claims 88, 99, and 102-110 all require, among other elements, that the non-oligomerizing tandem fluorescent protein of the claim comprise a mutation of an amino acid residue corresponding to A206K, L221K, F223R, or a combination thereof of SEQ ID NO: 6 or SEQ ID NO:10. Prasher nowhere discloses a mutation of an amino acid residue corresponding to A206K, L221K, F223R, or a combination thereof of SEQ ID NO: 6 or SEQ ID NO:10. Accordingly, Prasher does not anticipate Claims 88, 93, 99, and 102-110.

Claims 88, 93, 99, 102-110, 128 and 134 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Heim. Claims 88, 99, and 102-110 include the elements discussed above, with claim 93 being canceled. Claims 128 and 134 depend from Claim 88, and also require all the elements of Claim 88. However, Heim nowhere discloses a mutation of an amino acid residue corresponding to A206K, L221K, F223R, or a combination thereof of SEQ ID NO: 6 or SEQ ID NO:10. Accordingly, Heim does not anticipate Claims 88, 93, 99, 102-110, 128 and 134.

Claims 88, 93-95, 99, 102-110, 128 and 134 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by Tsien. Claims 93-95 stand canceled in the present application. Claims 88, 99, 102-110, 128 and 134 include the elements discussed above. However, Tsien nowhere discloses tandem fluorescent proteins including a mutation of an amino acid residue corresponding to A206K, L221K, F223R, or a combination thereof of SEQ ID NO: 6 or SEQ ID NO:10. Accordingly, Tsien does not anticipate Claims 88, 93-95, 99, 102-110, 128 and 134.

Accordingly, in the absence of disclosure regarding at least these elements of the claimed invention, applicants respectfully submit that the rejections under 35 U.S.C. §102 are overcome.

### **CONCLUSION**

Applicants respectfully submit that all claim rejections and objections are overcome by the above arguments and amendments, and request reconsideration and

allowance of Claims 88, 96, 98, 99, 102-110, 128, 134, 138, and 154-156. An early indication of their allowance is earnestly requested. The Examiner is invited to contact the undersigned attorney at the telephone number indicated below should he find that there are any further issues outstanding.

Although no fees are believed to be due at this time, please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 08-1641 referencing Attorney's Docket No. 39754-0831 CP2.

Respectfully submitted,



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